UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SOPHIE CHEN

Appeal No. 2006-3290
Application No. 10/072,823

ON BRIEF

Before SCHEINER, ADAMS and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from Examiner's final rejection of claims 1-9, 11-16, 18-23, 26-29 and 32-35, which are all the claims pending in the application.

Claim 1[1] is illustrative of the subject matter on appeal and is reproduced below:

1. A composition for treating or preventing prostate cancer or breast cancer [comprising]:
oridonin, a pharmaceutically acceptable salt or ester of oridonin, a selectively substituted analog of oridonin, or a combination thereof; and
lupulone, a pharmaceutically acceptable salt or ester of lupulone, a selectively substituted analog of lupulone, or a combination thereof;
wherein the composition is suitable for the treatment or prevention of prostate cancer or breast cancer.

[1] The remaining claims depend directly or indirectly from claim 1.

The references relied upon by Examiner are:

Fujita et al. ('016)	UK 1 476 016	Jun. 10, 1977
Fujita et al. ('434)	JP S52-102434	Aug. 27, 1977
Matsui	JP Sho 52-145509	Dec. 3, 1977
Son et al. (Son)	JP Sho 57-167938	Oct. 16, 1982
Ito et al. (Ito)	JP H11-236334	Aug. 31, 1999

GROUND OF REJECTION

Claims 1-9, 11-16, 18-23, 29-29 and 32-35 stand rejected under 35 U.S.C. § 103 as being unpatentable over the combination of any one of Son, '016 or '434 with either Ito or Matsui.

We affirm.

CLAIM GROUPING

Appellant does not separately group or argue the claims. Accordingly, the claims will stand or fall together. Therefore, we limit our discussion to representative independent claim 1. Claims 2-9, 11-16, 18-23, 26-29 and 32-35 will stand or fall together with claim 1. 37 C.F.R. § 41.37(c)(1)(vii) (July 2005).

DISCUSSION

Claim Construction:

Claim 1 is drawn to a composition that comprises two components:

(1) oridonin, a pharmaceutically acceptable salt or ester of oridonin, a selectively substituted analog of oridonin, or a combination thereof; and

(2) lupulone, a pharmaceutically acceptable salt or ester of lupulone, a selectively substituted analog of lupulone, or a combination thereof.

While the preamble of claim 1 contains language regarding the intended use of the composition "for treating or preventing prostate cancer or breast cancer," we do not find this language to be a limitation on the claim. Rowe v. Dror, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997) ("Where . . . a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation.").

In addition, claim 1 requires that "the composition is suitable for the treatment or prevention of prostate cancer or breast cancer." In our opinion, this clause is a statement of the intended use of the composition and only requires that the composition may be used for the treatment or prevention of prostate cancer or breast cancer. The composition itself may be "suitable" for a variety of uses.

Obviousness:

Examiner finds that Son, '434 or '016 teach compositions comprising oridonin. Answer, page 4. Examiner finds that Son, '434 and '016 teach that oridonin is useful to treat cancer.[2] Id. In addition to the treatment of cancer, Son and '016 also teach the use of oridonin for the treatment of, inter alia, oral diseases and sore throat (Son, bridging sentence, pages 4-5), stomachache

[2] Appellant concedes that '016 and '434 teach "pharmaceutical compositions comprising oridonin . . . as antitumor agents"; and Son teaches "that oridonin is known to exhibit carcinostatic activity." Brief, page 5. Appellant states that "[c]arcinostatic activity refers to the ability of oridonin to stop the growth of cancer." Brief, bridging sentence, pages 5-6.

('016, page 1) and gastrointestinal disorders ('016, page 1). Son, '434 and '016 do not teach a composition comprising lupulone.

Examiner finds that Ito and Matsui teach Humulus lupulus extracts that are useful for treating cancer.[3] Answer, page 4. Page 2 of Appellant's specification discloses that lupulone is known to be present in extracts of Humulus lupulus hops. Answer, page 4. In addition to the treatment of cancer Matsui teach that a hop extract comprising lupulone "has an efficacy on . . . gastroenteric trouble." Matsui, page 10. Ito and Matsui do not teach a composition comprising oridonin.

Based on this evidence, Examiner finds (Answer, page 5), "since each component is known individually in the prior art for the same purpose, i.e. to treat cancer, then it would have been obvious to combine the two components into one formulation." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) ("it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose"); In re Susi, 440 F.2d 442, 445, 169 USPQ 423, 426 (CCPA 1971) ("the combination, for the same purpose, of one additive explicitly disclosed in the prior art and another suggested by the prior art would be at least prima facie obvious"); In re Crockett, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960) ("the idea of combining them [magnesium oxide and calcium carbide] would flow logically from the

[3] Appellant concedes that Ito teaches Humulus lupulus extracts as cancer metastasis inhibitors; and Matsui "alleges that 'a bitter principle of hops of Humulus lupulus [sic],' prepared by aqueous extraction of dried hops, exhibits an anti-cancer effect for cancers of the stomach, liver, lung, and breast." Brief, page 6.

teaching of the prior art and therefore . . . a claim to their joint use is not patentable").

Appellant asserts that Matsui produces aqueous hop extracts and "there are active components in hops such as lupulone which cannot be extracted by water and can only be extracted by alcohol or organic solvents. Thus it is not clear if the extract in this reference actually contains lupulone." Brief, page 6. Appellant does not, however, direct our attention to any evidentiary basis to support this assertion.[4] Accordingly, we do not find this assertion persuasive.

Ito teaches that the active ingredient of Humulus lupulus can be extracted with either an organic solvent (e.g., methanol) or with water. See Ito, paragraphs 37 and 49-52. See also paragraph 68 (50% ethanol extract of hops). There is no evidence on this record to suggest that this active ingredient is not lupulone. See Answer, page 4, where Examiner reasons since lupulone is "known in the art to be in extracts of Humulus lupulus" there is no reason to expect that it would not be present in the extracts taught by Ito and Matsui. Accordingly, we are not persuaded by Appellant's intimation that since Ito and Matsui fail to describe the chemical contents of the extracts there is no evidence that lupulone is present in the extracts of Ito and Matsui. Brief, page 6.

[4] Attorney argument cannot take the place of evidence lacking in the record. Meitzner v. Mindick, 549 F.2d 775, 782, 193 USPQ 17, 22 (CCPA 1977).

Appellant asserts that '016, '434, Son or Ito do not teach the type of cancer that can be treated with the compound or extract. Brief, pages 5-6.[5] However, as discussed above, there is no requirement in Appellant's claim 1 that cancer generally or any particular type of cancer be treated. As set forth in In re Pearson, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974), "terms [that] merely set forth the intended use for ... an otherwise old composition ... do not differentiate the claimed composition from those known in the prior art." The Pearson court explained that "[i]t seems quite clear to us that one of the compositions admitted to be old by the appellant would not undergo a metamorphosis to a new composition by labeling its container to show that it is a composition suitable for [another use]." Id. The evidence of record establishes that both oridonin and lupulone are individually effective for the treatment of gastrointestinal disorders (stomachache). See '016, page 1 (oridonin) and Matsui, page 10 (lupulone). Accordingly, we find that the evidence of record establishes that a person of ordinary skill in the art would have been motivated to combine oridonin and lupulone into a composition for the treatment of gastrointestinal disorders. See Kerkhoven, Susi, and Crockett.

Nevertheless, since the record before us is focused on the combination of the references for the treatment of cancer we will address this issue. Appellant contends that "[t]he cited references do not provide the motivation to combine oridonin and lupulone to treat the same types of cancers, let alone breast and

[5] Appellant recognizes that '016, '434, Son and Ito do not teach the treatment of any particular cancer. Nevertheless, Appellant asserts (Brief, page 9), "[b]ased on the references cited by the Examiner, there appears to be no overlap between the cancer-type specificity of oridonin and lupulone." What is unclear on this record is how Appellant can reach this conclusion when she recognizes that four of the five references relied upon teach a non-specific anti-cancer activity.

prostate cancer." Brief, page 7. Appellant relies on four exhibits submitted with the response received May 7, 2004 to develop this point. Directing attention to Exhibit 1[6], Appellant asserts (Brief, page 9), "[i]t is well known in the pharmaceutical arts that different types of cancer respond differently to different anticancer agents." Exhibit 1 does contain a single sentence that states in part "there are more than a hundred distinct types of cancer, which can vary substantially in their behavior and response to treatment." Exhibit 1 does not, however, identify which types of cancers do respond differently to treatment or which types of treatments result in different cancer type responses.

In contrast, Ito teaches that "[t]he plants [from which the Lupulone extract is derived] . . . are widely used for their effectiveness in the prevention and therapy of cancer." Ito, paragraph 46. Similarly, Matsui teaches that "the cancer treating drug [(lupulone)] manufactured from the nontoxic harmless hops . . . exerted excellent effects on the treatment of various kinds of cancers such as stomach cancer, bladder cancer, and liver cancer." Matsui, bridging paragraph, pages 10-11, emphasis added. We find nothing in Ito or Matsui to suggest that the anti-cancer activity of lupulone is restricted to a particular type of cancer. The same is true of Son, '434 and '160. See e.g., '434, page 4, "the invention [(oridonin)] offers a new and effective carcinostatic agent that demonstrates an excellent life extending effect on cancer patients"; and '016, page 3, "[t]his invention . . . provides the new and useful anti-tumor agents [(e.g., oridonin)] which . . . are expected to be effective for several other tumors including cancer."

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[6] THE CELL A MOLECULAR APPROACH p. 610 (Geoffrey M. Cooper, ed., 2nd ed., ASM Press, Washington, D.C. 2000).

Notwithstanding Appellant's argument to the contrary, we find nothing in the evidence of record to suggest that the activity of oridonin and lupulone is limited to any particular type of cancer. Instead, the evidence of record suggests that lupulone and oridonin exhibit their activity against cancers generally. Therefore, a person of ordinary skill in the art would have been led to combine lupulone and oridonin to make a composition that would be suitable for the treatment of cancers generally.

With reference to Exhibit 2[7], Appellant asserts "[t]he type of treatment used to treat cancer depends, in part, on the type of cancer to be treated." Brief, page 9. Therefore Appellant contends that "[c]ombinations of anticancer agents should be chosen, at least in part, based on the type of cancer to be treated." Id. Exhibit 2 discusses a variety of cancer treatments and states (page 1, paragraph 4), "[t]he type of chemotherapy given depends on the type of cancer you have[,] the stage of your cancer, and your overall health." Exhibit 2 also states (page 1, paragraph 2), "[c]hemotherapy drugs destroy cancer cells by stopping them from growing and multiplying. However, healthy cells can also be harmed, especially those that divide quickly, such as white blood cells." Appellant has failed to establish that a person of ordinary skill in the art would consider oridonin and lupulone to be included in the class of "chemotherapy drugs" discussed in Exhibit 2.

In contrast, Ito points out (paragraph 7), "it has been found that there are hardly any adverse reactions from herbal medicine oriented plants, they are

[7] http://www.bymyside.com/treatment/types_treatment.jsp.

presented as drug products, non-drug products, and food products for possible long term use." All of the references relied upon by Examiner teach oridonin or lupulone extracts from herbal medicine oriented plants. Ito distinguishes drugs from herbal medicine oriented plants from "strong drugs with adverse reactions [which] are used in the treatment of cancer . . . ." Therefore, unlike Exhibit 2's reference to chemotherapeutics that have a harmful effect on healthy cells, the references relied upon by Examiner teach that oridonin is a "safe and effective" agent (see e.g., '434, page 3 and '016, page 3); lupulone "is nontoxic and harmless to the human body" (Matsui, page 10); and "it is known that the safety of these plants and extracts is high" (Ito, paragraph 41).

Regarding the combination of oridonin and lupulone in a composition to treat cancer, Ito teaches (paragraph 6), "[t]hese metastasis control substances [(e.g., lupulone)] are used as complementary treatment agents for controlling the metastasis before and after surgery or radiation treatment, and it is expected they will also find use as a combination therapy agent." According to Ito (paragraph 43), "[t]here is no special limitation for other cited additives" when lupulone is "used for preparation of the usual drugs, non-drugs, food products . . . ." Therefore, contrary to Appellant's assertion, Ito provides evidence to suggest that lupulone can be combined with a variety of other ingredients without adverse effect. Given that the references relied upon teach that oridonin and lupulone have no harmful effect when administered, and the suggestion that lupulone can be used as a complementary or combination drug, we find no error in Examiner's assertion that it would have been prima facie obvious to combine oridonin and

lupulone into a composition for the treatment of cancer. Answer, page 5. Accordingly, we are not persuaded by Appellant's argument.

The same is true of Appellant's argument relating to Exhibit 3[8] and Exhibit 4[9]. With reference to Exhibit 3 Appellant asserts "that optimization of drug combinations is not straight forward and in fact requires 'clinical empiricism and trial and error'." Brief, page 9. Appellant, however, fails to acknowledge that this statement was made with respect to a specific cancer – childhood acute lymphoblastic leukemia (ALL). According to Exhibit 3 (page 1, second paragraph, endnotes omitted),

> childhood acute lymphoblastic leukemia (ALL), a disease that 25 years ago claimed the lives of the majority of ALL patients . . . today is up to 90% curable. Over that 25-year period, no new drugs have entered standard treatment protocols; rather, it has been the optimization of combinations of old drugs, based entirely on clinical empiricism and trial and error, that has yielded such effective results.

We find no suggestion in the reference that this statement applies to the treatment of cancers generally, or to the class of compounds[10] taught by the references before us on appeal. Accordingly, we are not persuaded by Appellant's argument.

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[8] http://www.nature.com/cgi-taf/DynaPage.taf?file=/nm/journal/v9/n5/full/nm0503-510.html. We note that this website directs attention to the following article: Golub, "Mining the genome for combination therapies," Nature, Vol. 9, No. 5, pp. 510-511 (2003).

[9] Johnson et al. (Johnson), "Antagonistic Interplay between Antimitotic and G_1-S Arresting Agents Observed in Experimental Combination Therapy," Clin. Cancer Res., Vol. 5, pp. 2559-2565 (1999).

[10] In this regard, we note that Exhibit 3 discusses combination therapy using mercaptopurine and methotrexate. Appellant makes no attempt to establish that these are the same class of compounds as oridonin and lupulone.

Regarding Exhibit 4, Appellant asserts that "combinations of anti-cancer agents can in fact have negative effects." Brief, page 5. According to Appellant, Exhibit 4 reports that "antimitotic agents such as paclitaxel and G_1-S arresting agents such as 5-fluorouracil have antagonistic effects." From this Appellant argues that since the "references provided by Examiner provide no suggestion as to the mechanism of action of lupulone and oridonin . . . there is no motivation to combine and no expectation of success for this combination." Reply Brief, bridging paragraph, pages 5-6. We are not persuaded by Appellant's argument.

Despite Appellant's emphasis on the antagonistic effects of paclitaxel and 5-fluorouracil in the treatment of cancer, we note that Exhibit 4 teaches that as of the publication date of the reference clinical trials were being performed with combinations of paclitaxel and 5-fluorouracil. Exhibit 4, page 2559, column 2, first full paragraph. Therefore, the teachings of the reference itself run counter to the emphasis Appellant places on the reference. Further, contrary to Appellant's intimation, the antagonistic effects discussed in Exhibit 4 are not as absolute as Appellant would lead us to believe. See e.g, Exhibit 4's conclusion that "[o]ur results demonstrate that both 5-FU [5-fluorouracil] and HU [hydroxyurea] could interfere with the cytotoxic effects of antimitotic agents on mitotic arrest and apoptosis." Exhibit 4, page 2564, second column, first paragraph, emphasis added.

In our opinion the evidence relied upon by Examiner provides a reasonable expectation of formulating a composition comprising lupulone and oridonin. That Exhibit 4 suggests the possibility that some compounds could

have antagonizing activities when used in combination does not detract from the reasonable expectation of success in combining lupulone and oridonin as set forth in the rejection of record. "Only a reasonable expectation of success, not absolute predictability, is necessary for a conclusion of obviousness." In re Longi, 759 F.2d 887, 897, 225 USPQ 645, 651-52 (Fed. Cir. 1985). Accordingly, we disagree with Appellant's assertion that there is "no expectation of success for this combination." Reply Brief, page 5.

On reflection, it is our opinion that the weight of the evidence on this record falls in favor of Examiner. Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. § 103 as being unpatentable over the combination of any one of Son, '016 or '434 and either Ito or Matsui. Claims 2-9, 11-16, 18-23, 26-29 and 32-35 fall together with claim 1.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Toni R. Scheiner
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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